# Small Intracranial Aneurysms: Diagnostic Accuracy of CT Angiography[1]

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**Purpose:** To assess the accuracy of computed tomographic (CT) angiography for diagnosis of cerebral aneurysms 5 mm or smaller, with digital subtraction angiography (DSA) as the reference standard, in a large patient cohort

**Materials and Methods:** This retrospective study was approved by the local institutional review board with a waiver of written informed consent. A total of 1366 patients who underwent cerebral CT angiography followed by DSA were included. The performance of CT angiography for depiction of aneurysms was evaluated by two readers on a per-patient and per-aneurysm basis and based on size of aneurysm, location, and status of rupture. The performance of CT angiography for diagnosis of aneurysms of different size, location, and rupture status was compared by using $\chi^2$ test. κ statistic was used to assess interreader agreement for diagnosis of aneurysms.

**Results:** Of 1366 patients, 579 patients had 711 small aneurysms at DSA. By using DSA as the reference standard, the respective sensitivity, specificity, and accuracy of CT angiography for readers 1 and 2 for detection of small aneurysms on a per-patient basis were 97.1% (562 of 579) and 97.4% (564 of 579), 98.5% (451 of 458) and 99.1% (454 of 458), and 97.7% (1013 of 1037) and 98.2% (1018 of 1037) and those on a per-aneurysm basis were 95.2% (677 of 711) and 95.4% (678 of 711), 96.6% (451 of 467) and 97.0% (454 of 468), and 95.8% (1128 of 1178) and 96.0% (1132 of 1179). The sensitivities of CT angiography were lower for detection of aneurysms smaller than 3 mm and unruptured compared with aneurysms that were 3–5 mm and ruptured ($P < .001$). No difference existed for the sensitivities of CT angiography for diagnosis of aneurysms in the anterior versus posterior circulation ($P > .0167$). Excellent or good interreader agreement was found for detection of intracranial aneurysms on a per-patient (κ = 0.982) and per-aneurysm (κ = 0.748) basis.

**Conclusion:** This large cohort study demonstrated that CT angiography had high accuracy for detection of small cerebral aneurysms, including those smaller than 3 mm.



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The prevalence of cerebral aneurysms in the general population is approximately 2%–3% (1–3). About 80%–85% of nontraumatic subarachnoid hemorrhages are caused by cerebral aneurysm rupture (4), which is a serious vascular event with a high mortality rate (5,6). Small cerebral aneurysms are generally defined as aneurysms with a diameter of 5 mm or less (7). Previous studies (8–11) showed that many small cerebral aneurysms have a low risk of rupture. Observation is often the preferred course of treatment in selected patients with small unruptured intracranial aneurysms (12) because treatment-related morbidity and mortality are often greater than or equal to the risk of the aneurysm rupturing (13,14). Therefore, a convenient and accurate imaging modality to detect and monitor small intracranial aneurysms is desired.

Computed tomographic (CT) angiography is a noninvasive, convenient, and reliable modality to help detect and triage the management of intracranial aneurysms (15–17). Previous studies (18–21) evaluated the performance of cerebral CT angiography for depiction of intracranial aneurysms; however, the results remain controversial. In a study by Lu et al (15), 513 participants underwent first-generation dual-source CT angiography, which showed excellent diagnostic accuracy for detection of cerebral aneurysms with different sizes, even those smaller than 5 mm. Meanwhile, a recent prospective observational study (18) that included 179 patients with 99 small intracranial aneurysms (<3 mm) reported that the sensitivity of CT angiography for diagnosis of intracranial aneurysms 3 mm or smaller was 28%–43% by using 64–256-section multi–detector row CT scanners. The discrepancy between the results of these previous studies caused the American Heart Association to state in 2014 that cerebral CT angiography was inadequate for evaluation of aneurismal subarachnoid hemorrhages because it is less accurate in detecting small cerebral aneurysms, especially those smaller than 3 mm (22). A small sample size may have been an important factor that resulted in the discrepant findings with CT angiography for detection of small intracranial aneurysms. Thus, a comparison study with a large cohort seems desirable to determine the role of CT angiography in detection of small cerebral aneurysms. The purpose of this study was to assess the accuracy of CT angiography for diagnosis of cerebral aneurysms 5 mm or smaller, with digital subtraction angiography (DSA) as the reference standard, in a large patient cohort.

## Advance in Knowledge

- Cerebral CT angiography had excellent diagnostic accuracy (95.8% [1128 of 1178] and 96.0% [1132 of 1179] for two readers, respectively) for detection of small intracranial aneurysms with a per-aneurysm analysis compared with digital subtraction angiography.

## Implication for Patient Care

- Cerebral CT angiography is a valuable technique for detecting and following small intracranial aneurysms, especially for ruptured aneurysms.

## Materials and Methods

U.J.S. is a consultant for and/or receives research support from Astellas, Bayer, Bracco, GE, Guerbet, Medrad, and Siemens. The other authors controlled the data and the information submitted for publication.

### Patients

This retrospective study was approved by the institutional review board of Jinling Hospital, Medical School of Nanjing University, Nanjing, China, with a waiver of written informed consent. A total of 1486 patients (45.1% [670 of 1486] men; mean age, 50.6 years ± 13.8 [standard deviation]) who had known or were suspected of having cerebrovascular disease underwent both head DSA and CT angiography at our institution between June 2009 and April 2016. The main inclusion criterion stipulated that patients had undergone cerebral CT angiography and subsequent DSA. The exclusion criteria consisted of the following: patients who underwent DSA before head CT angiography, which was used as a surveillance tool for the patients with initial DSA image negative for aneurysms or with small unruptured intracranial aneurysms ($n = 34$); patients with more than a 1-month interval between CT angiography and DSA ($n = 81$); patients with incomplete image data because of failed image archiving ($n = 5$); and known or treated aneurysms (as a per-aneurysm exclusion). As a result, 1366 patients (44.9% [613 of 1366] men; mean age, 50.8 years ± 13.7) were included in this study. Of the 1366 patients, 1187 (86.9% [1187 of 1366]) had an intracranial hemorrhage. Figure 1 displays the flowchart of this retrospective study.

### Image Acquisition

*Cerebral CT angiography acquisition.*—All cerebral CT angiographic examinations were performed by one of two dual-source CT systems (Somatom Definition or Somatom Definition Flash; Siemens Healthcare, Forchheim, Germany). Conventional CT imaging that

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Abbreviations:
DSA = digital subtraction angiography
3D = three-dimensional

Author contributions:
Guarantors of integrity of entire study, Z.L.Y., Q.Q.N., G.M.L., L.J.Z.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; agrees to ensure any questions related to the work are appropriately resolved, all authors; literature research, Z.L.Y., Q.Q.N., U.J.S., C.N.D.C., H.L., T.M.D., Y.E.Z., G.M.L., L.J.Z.; clinical studies, Z.L.Y., Q.Q.N., H.L., C.S.Z., L.J.Z.; experimental studies, Q.Q.N., H.L.; statistical analysis, Z.L.Y., Q.Q.N., H.L., T.M.D., C.S.Z., Y.E.Z., L.J.Z.; and manuscript editing, Z.L.Y., Q.Q.N., U.J.S., C.N.D.C., H.L., T.M.D., G.M.L., L.J.Z.

Conflicts of interest are listed at the end of this article.

**Figure 1**

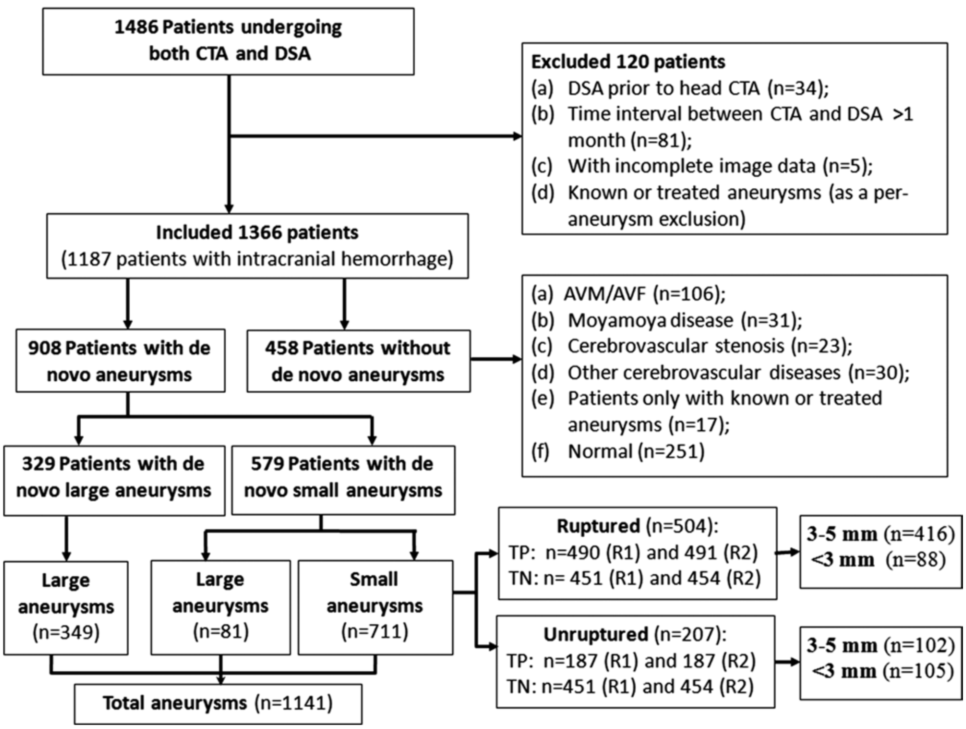


**Figure 1:** Study flowchart. *CTA* = CT angiography, *AVM/AVF* = arteriovenous malformation/fistula, *R1* = reader 1, *R2* = reader 2, *TN* = true-negative finding, *TP* = true-positive finding.

was not contrast agent enhanced was performed at 120 kVp and 140–180 mAs. Images were acquired with a collimation of 64 × 0.6 mm or 64 × 2 × 0.6 mm, a rotation time of 0.5 second, and a pitch of 1.2. All images were reconstructed by using I26f/H26f kernels (Siemens Healthcare) with a section thickness of 0.75 mm and an increment of 0.5 mm. Contrast-enhanced CT angiography was subsequently performed. Sixty milliliters of the iodinated contrast agent iopromide (300 mg of iodine per milliliter, Ultravist 300; Bayer Schering, Berlin, Germany) was injected into the antecubital vein at 4.0 mL per second for each patient, followed by a 30-mL saline solution injection at the same rate via a 22-gauge catheter. We used a bolus-tracking technique to trigger automatic CT scanning by placing a region of interest in the proximal segment of the internal carotid artery. CT scanning began 3 seconds after the attenuation of the region of interest had reached the predefined threshold of 100 HU with a scanning time of 3–5 seconds. The scanning protocols for contrast-enhanced CT angiography were as follows: tube voltage, 120 kVp; effective tube current, 140–180 mAs; collimation, 64 × 0.6 mm or 64 × 2 × 0.6 mm; rotation time, 0.5 second; and pitch, 1.2. The volumetric CT dose index and dose-length product of volume CT for the whole CT angiographic examination were 21.9–29.6 mGy and 418–585 mGy · cm, respectively.

*DSA acquisition.*—Head DSA was performed with a biplane DSA unit with rotational capability (Axiom Artis dTA; Siemens). By using the Seldinger technique for femoral catheterization, a catheter was placed in bilateral internal carotid arteries and unilateral or bilateral vertebral arteries for angiography. A standard acquisition was performed by using 6–9 mL of iopromide (300 mg of iodine per milliliter, Ultravist 300; Bayer Schering) at an injection rate of 4.0–5.0 mL/sec and it included one anteroposterior, one lateral, and one or two oblique views with a 1024 × 1024 matrix. The fields of view were 38 cm$^2$, 30 cm$^2$, and 30 cm$^2$ for anteroposterior, lateral, and oblique images, respectively. If an initial DSA did not help to determine a suspected cerebral aneurysm, a rotational angiographic examination was usually performed before removing the catheter from the vessel. The three-dimensional (3D) DSA image was obtained by injecting 16–20 mL of contrast agent at a rate of 4.0 mL/sec with a rotation arch of 240°. The 3D images were immediately analyzed by using a 3D workstation (Siemens Healthcare).

## Image Review

*Cerebral CT angiography review.*—Acquired CT image series were automatically transferred to a dedicated workstation for review (Multi Modality Workplace; Siemens Healthcare). CT angiography images were generated with a workstation (Syngo 2008G; Siemens) with the bone voxels removed by software (Neuro DSA application) and were reformatted with software (Syngo InSpace, Siemens) at a 3D workstation. Two neuroradiologists (L.J.Z. and Q.Q.N., with 16 and 2 years of neuroimaging experience, respectively) who were blinded to clinical information and DSA results independently analyzed all cerebral CT angiography images by using source images, maximum intensity projections, multiplanar reformations, and volume-rendering reformatted images to determine the presence and locations of aneurysms. On images where aneurysms were visible, the maximal diameter was measured. The following locations of cerebral arteries were recorded: bilateral internal carotid arteries, bilateral anterior cerebral arteries, bilateral middle cerebral arteries, anterior communicating arteries, bilateral posterior communicating arteries, bilateral posterior cerebral arteries, vertebral and basilar arteries, and bilateral cerebellar arteries, which encompassed bilateral posterior inferior cerebellar arteries, anterior inferior cerebellar arteries, and superior cerebellar arteries. Aneurysms in branch arteries or small distal vessels were included with the corresponding main cerebral artery. For example, aneurysms at pericallosal or callosomarginal arteries were regarded as aneurysms in the anterior cerebral artery. Known or treated aneurysms were excluded when analyzed. Reviewers were allowed to adjust, rotate, and reformat 3D images at the workstation to optimally view the presence and location of an individual aneurysm. If a lesion was highly suspicious for aneurysm, target vessel reformation was performed at the workstation by removing other redundant vessels. For unilateral internal carotid artery aneurysm, the readers removed the contralateral internal carotid artery system and the posterior circulation system, whereas we removed the anterior circulation system in the posterior circulation arteries. Additionally, the readers adjusted the window setting and zoomed the images to optimally view the aneurysm. To evaluate the interreader agreement of CT angiography image quality, the same two neuroradiologists independently evaluated image quality in 100 patients randomly selected from our patient cohort by using a four-point scale: score of 4, excellent; score of 3, good; score of 2, acceptable; score of 1, nondiagnostic (23). They also recorded the presence or absence of intracranial hemorrhage, which included nontraumatic subarachnoid hemorrhage and brain parenchyma hemorrhage consistently for each patient.

*DSA review.*—All DSA datasets were transferred to a 3D workstation (Siemens). Two interventional neuroradiologists (not authors; both with more than 10 years of experience) reviewed all two-dimensional and 3D DSA images and made a consensus diagnosis. They had access to clinical and imaging information, including CT angiography images and CT angiography reports. In cases with aneurysms, the maximal diameter was measured and the location of each aneurysm was recorded. Reviewers also determined whether an aneurysm was ruptured or unruptured according to clinical and imaging information. Locations of aneurysms were classified as the anterior circulation system, which included bilateral internal carotid artery, bilateral anterior cerebral artery, bilateral middle cerebral artery, anterior communicating artery, and bilateral posterior communicating artery; and the posterior circulation system, which included bilateral posterior cerebral artery, vertebral and basilar artery, and bilateral cerebellar artery, as described in the cerebral CT angiography review section.

### Statistical Analysis

Statistical analysis was performed by using statistical software (SPSS, version 20.0; SPSS, Chicago, Ill). With DSA as the reference standard, the sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of CT angiography for evaluation of small intracranial aneurysms were calculated on a per-patient and per-aneurysm basis with a 95% confidence interval by using the Wilson score method. By considering the inherent clustering and correlation by patient, we adjusted the 95% confidence intervals of sensitivities and specificities on a per-aneurysm analysis by using a ratio estimator (24), and when the sensitivities or specificities were 100%, the confidence intervals were not adjusted. The performance of CT angiography for depiction of aneurysms that were different sizes (<3 mm and 3–5 mm) and locations (anterior and posterior circulation) was compared by using the $\chi^2$ test. We also compared the performance of CT angiography for detection of cerebral aneurysms with a per-patient analysis (with and without cerebral hemorrhage) and with a per-aneurysm analysis (ruptured and unruptured) with $\chi^2$ test. Cohen $\kappa$ analysis was used to assess interreader agreement for detection of cerebral aneurysms with CT angiography on a per-patient and per-aneurysm basis ($\kappa$ = 0, poor agreement; $\kappa$ = 0.01–0.20, slight agreement; $\kappa$ = 0.21–0.40, fair agreement; $\kappa$ = 0.41–0.60, moderate agreement; $\kappa$ = 0.61–0.80, good agreement; and $\kappa$ = 0.81–1.00, excellent agreement) (15). $P$ values of .05 or less were considered to indicate statistical significance. For comparison of sensitivity, specificity, negative predictive value, positive predictive value, and accuracy of CT angiography for detection of aneurysms (<3 mm vs 3–5 mm, anterior circulation vs posterior circulation aneurysms, and ruptured vs unruptured aneurysm), we used a stricter threshold for $P$ values of .0167 or less (.05/3 = .0167).

## Results

### Patients and Aneurysms

Of 1366 patients, 458 patients (59.0% [270 of 458] men; mean age, 44.9 years ± 16.1) had no de novo cerebral aneurysms at DSA (Fig 1). At DSA, 908 patients (37.9% [344 of 908] men; mean age, 53.6 years ± 11.4) had 1141 de novo cerebral aneurysms, including 430 large aneurysms and 711 small aneurysms (Fig 1, Table 1). There were 329 patients (38.0% [125 of 329] men; mean age, 54.3 years ± 11.4) with 349 de novo aneurysms larger than 5 mm in diameter. DSA helped to depict 711

**Table 1**

**Diagnostic Performance of CT Angiography in Detecting Small Cerebral Aneurysms on a Per-Aneurysm Basis**

| Parameter | Results (No. of Aneurysms) | | | | Test Performance (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | TP | TN | FP | FN | Sensitivity | Specificity | PPV | NPV | Accuracy |
| Overall | | | | | | | | | |
| R1 | 677 | 451 | 16 | 34 | 95.2 (677/711) [93.8, 96.7] | 96.6 (451/467) [94.8, 98.3] | 97.7 (677/693) [96.3, 98.6] | 93.0 (451/485) [90.4, 94.9] | 95.8 (1128/1178) [94.5, 96.8] |
| R2 | 678 | 454 | 14 | 33 | 95.4 (678/711) [93.7, 97.0] | 97.0 (454/468) [95.5, 98.6] | 98.0 (678/692) [96.6, 98.8] | 93.2 (454/487) [90.6, 95.1] | 96.0 (1132/1179) [94.7, 97.0] |
| Aneurysms 3–5 mm | | | | | | | | | |
| R1 | 506 | 451 | 7 | 12 | 97.7 (506/518) [96.4, 99.0] | 98.5 (451/458) 97.3, 99.6] | 98.6 (506/513) [97.2, 99.3] | 97.4 (451/463) [95.5, 98.5] | 98.1 (957/976) [97.0, 98.8] |
| R2 | 510 | 454 | 8 | 8 | 98.5 (510/518) [97.2, 99.7] | 98.3 (454/462) [97.1, 99.5] | 98.5 (510/518) [97.0, 99.2] | 98.3 (454/462) 96.6, 99.1] | 98.4 (964/980) [97.4, 99.0] |
| Aneurysms <3 mm | | | | | | | | | |
| R1 | 171 | 451 | 9 | 22 | 88.6 (171/193) [84.0, 93.2] | 98.0 (451/460) [96.6, 99.4] | 95.0 (171/180) [90.8, 97.4] | 95.3 (451/473) [93.1, 96.9] | 95.3 (622/653) [93.3, 96.6] |
| R2 | 168 | 454 | 6 | 25 | 87.0 (168/193) [81.6, 92.5] | 98.7 (454/460) [97.7, 99.7] | 96.6 (168/174) [92.7, 98.4] | 94.8 (454/479) [92.4, 96.4] | 95.3 (622/653) [93.3, 96.6] |

Note.—Data in parentheses are numerator and denominator; data in brackets are 95% confidence intervals. FN = false-negative finding, FP = false-positive finding, NPV = negative predictive value, PPV = positive predictive value, R1 = reader 1, R2 = reader 2, TN = true-negative finding, TP = true-positive finding.

small and 81 large cerebral aneurysms in 579 patients (37.5% [217 of 579] men; mean age, 53.2 years ± 11.4). Of the 579 patients in whom DSA helped to detect small aneurysms, 488 patients had one small aneurysm, 65 patients had two small aneurysms, 17 patients had three small aneurysms, five patients had four small aneurysms, two patients had five small aneurysms, and two patients had six small aneurysms. Of 711 small cerebral aneurysms, 504 aneurysms were ruptured (<3 mm: 88 aneurysms, 17.5%; 3–5 mm: 416 aneurysms, 82.5%) and 207 aneurysms were unruptured (<3 mm: 105 aneurysms, 50.7%; 3–5 mm: 102 aneurysms, 49.3%). Of 711 small cerebral aneurysms, 639 (89.9%) aneurysms were located in the anterior circulation and 72 (10.1%) were located in the posterior circulation.

### Performance of CT Angiography on the Basis of Per-Patient Analysis

We rated 96.0% (96 of 100) of CT angiography examinations as good or excellent. Excellent or good interreader agreement was found on a per-patient basis ($\kappa$ = 0.982) and on a per-aneurysm basis ($\kappa$ = 0.748) for detection of intracranial aneurysms by using CT angiography.

With DSA as reference standard, the performances of CT angiography in detecting small aneurysms on a per-patient analysis including with or without cerebral hemorrhage are shown in Table 2. Table E1 (online) provides the diagnostic performance of CT angiography in detecting all cerebral aneurysms in a per-patient analysis including patients only with large aneurysms. No differences existed for the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of CT angiography in diagnosing aneurysms in patients with or without cerebral hemorrhage (all $P > .05$).

### Performance of CT Angiography on the Basis of Analysis per Aneurysm

Two readers detected 693 and 692 small aneurysms (180 and 174 <3 mm aneurysmsy; 513 and 518 3–5 mm aneurysms) with cerebral CT

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**Table 2**

**Diagnostic Performance of CT Angiography in Detecting Small Cerebral Aneurysms on a Per-Patient Basis**

| Parameter | Results (No. of Patients) | | | | Test Performance (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | TP | TN | FP | FN | Sensitivity | Specificity | PPV | NPV | Accuracy |
| Overall | | | | | | | | | |
| R1 | 562 | 451 | 7 | 17 | 97.1 (562/579) [95.4, 98.2] | 98.5 (451/458) [96.9, 99.3] | 98.8 (562/569) [97.5, 99.4] | 96.4 (451/468) [94.3, 97.7] | 97.7 (1013/1037) [96.6, 98.4] |
| R2 | 564 | 454 | 4 | 15 | 97.4 (564/579) [95.8, 98.4] | 99.1 (454/458) [97.8, 99.7] | 99.3 (564/568) [98.2, 99.7] | 96.8 (454/469) [94.8, 98.1] | 98.2 (1018/1037) [97.2, 98.8] |
| With intracranial hemorrhage | | | | | | | | | |
| R1 | 517 | 386 | 6 | 16 | 97.0 (517/533) 95.2, 98.1] | 98.5 (386/392) [96.7, 99.3] | 98.9 (517/523) [97.5, 99.5] | 96.0 (386/402) [93.6, 97.5] | 97.6 (903/925) [96.4, 98.4] |
| R2 | 519 | 388 | 4 | 14 | 97.4 (519/533) 95.6, 98.4] | 99.0 (388/392) [97.4, 99.6] | 99.2 (519/523) [98.1, 99.7] | 96.5 (388/402) [94.2, 97.9] | 98.1 (907/925) [96.9, 98.8] |
| Without intracranial hemorrhage | | | | | | | | | |
| R1 | 45 | 65 | 1 | 1 | 97.8 (45/46) [88.7, 99.6] | 98.5 (65/66) [91.9, 99.7] | 97.8 (45/46) [88.7, 99.6] | 98.5 (65/66) [91.9, 99.7] | 98.2 (110/112) [93.7, 99.5] |
| R2 | 45 | 66 | 0 | 1 | 97.8 (45/46) [88.7, 99.6] | 100 (66/66) [94.5, 100] | 100 (45/45) [92.1, 100] | 98.5 (66/67) [92.0, 99.7] | 99.1 (111/112) [95.1, 99.8] |

Note.—The analysis excludes patients with cerebral aneurysms larger than 5 mm. Data in parentheses are numerator and denominator; data in brackets are 95% confidence intervals. Total population, 1037 patients. Number of excluded patients, 329 patients. FN = false-negative finding, FP = false-positive finding, NPV = negative predictive value, PPV = positive predictive value, R1 = reader 1, R2 = reader 2, TN = true-negative finding, TP = true-positive finding.

angiography. With DSA as reference standard, the sensitivity, specificity, and accuracy of CT angiography for diagnosis of small cerebral aneurysms for the two readers were 95.2% (677 of 711) and 95.4% (678 of 711), 96.6% (451 of 467) and 97.0% (454 of 468), and 95.8% (1128 of 1178) and 96.0% (1132 of 1179), respectively. The performance of CT angiography to detect small cerebral aneurysms with different sizes is shown in Table 1. The sensitivity and accuracy of CT angiography for detection of aneurysms smaller than 3 mm were inferior to the results for aneurysms 3–5 mm ($P < .001$). The diagnostic performance of CT angiography in detecting aneurysms larger than 5 mm was excellent in general (Table E2 [online]); however, seven aneurysms larger than 5 mm were missed. Among these seven aneurysms, poor image quality at CT angiography was observed in three patients and dissecting aneurysms without an aneurysmal sac occurred in four patients. Figure 2 shows one representative case with three small cerebral aneurysms (including one ruptured and two unruptured aneurysms) correctly diagnosed by using CT angiography.

The performance of CT angiography to detect ruptured and unruptured small aneurysms with different sizes is provided in Table 3. The sensitivity of CT angiography to detect unruptured small aneurysms was lower than the sensitivity of CT angiography to detect ruptured small aneurysms ($P < .001$), whereas no significant differences were found for positive predictive value, negative predictive value, and accuracy ($P > .0167$).

### Performance of CT Angiography according to Aneurysm Locations

Two readers detected 625 and 624 small aneurysms in anterior circulation and 68 and 68 aneurysms in posterior circulation at cerebral CT angiography. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of CT angiography to help to diagnose small aneurysms with different locations are shown in Table 4. There were no differences for the sensitivity, positive predictive value, and

**Figure 2**

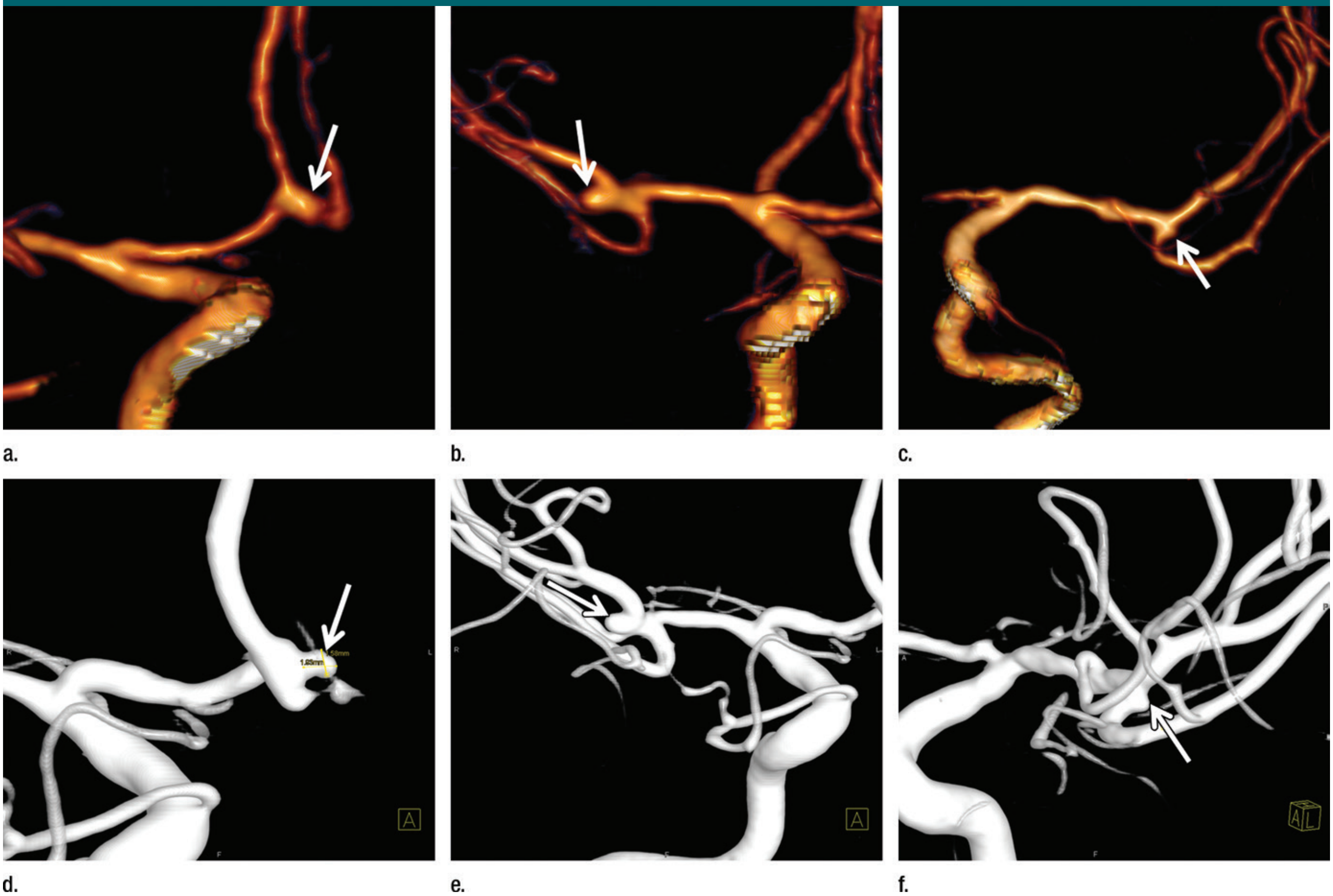

Figure 2: Three true-positive aneurysms in a 42-year-old woman. **(a–c)** Volume-rendered CT angiography images and **(d–f)** volume-rendered 3D DSA images show three small aneurysms. Two unruptured aneurysms in the right (2.18 mm; arrow, **b**, **e**) and left (1.3 mm; arrow, **c**, **f**) middle cerebral arteries and one ruptured aneurysm in the anterior communicating artery (maximum diameter of 1.93 mm, indicated in **d**; arrow, **a**, **d**) are clearly viewed on both CT angiography and 3D DSA images. *A* = anterior, *L* = left.

accuracy of CT angiography to diagnose small aneurysms located at anterior and posterior circulation ($P >$ .0167). The negative predictive value and specificity of CT angiography to help detect small aneurysms at posterior circulation were higher than those for detection of aneurysms at anterior circulation ($P <$ .0177). The sensitivity for detection of posterior cerebral artery aneurysms was 78.6% (11 of 14). The three missed aneurysms in the posterior cerebral artery were all smaller than 3 mm and located at the distal posterior cerebral artery (Fig E1 [online]). The diagnostic information at CT angiography for detection of aneurysms (including large and small aneurysms) with different sizes at anterior and posterior circulation is provided in Table E3 (online).

## False-Positive and False-Negative Findings

Reader 1 reported 16 false-positive small aneurysms in 15 patients (20% [three of 15] men) and missed 34 small aneurysms in 30 patients (56.7% [17 of 30] men), whereas reader 2 reported 14 false-positive small aneurysms in 13 patients (23.1% [three of 13] men) and missed 33 small aneurysms in 29 patients (48.3% [14 of 29] men) (Fig 3). Four small infundibula at branch vessel origins were diagnosed as small aneurysms and three false-positive aneurysms were observed in patients with other cerebrovascular diseases. A false-positive aneurysm (3.8 mm in size measured on a CT angiographic image) was observed at CT angiography at the right posterior inferior cerebellar artery in a 43-year-old male patient. The posterior inferior cerebellar artery could not be fully viewed on DSA images because right vertebral artery angiography and rotational 3D DSA were not performed in that patient (Fig 3a, 3b). More than a half (55.9% [19 of 34] and 57.6% [19 of 33] for readers 1 and 2, respectively) of false-negative small aneurysms occurred in patients with multiple aneurysms, whereas 64.7% (22 of 34) and 75.8% (25 of 33) missed aneurysms were smaller than 3 mm in diameter for readers 1 and 2, respectively. One of two adjacent aneurysms

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**Table 3**

**Diagnostic Performance of CT Angiography in Detecting Small Ruptured and Unruptured Cerebral Aneurysms**

| Parameter | Results (No. of Aneurysms) | | | | Test Performance (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | TP | TN | FP | FN | Sensitivity | Specificity | PPV | NPV | Accuracy |
| Ruptured small aneurysms | | | | | | | | | |
| Overall | | | | | | | | | |
| R1 | 490 | 451 | 15 | 14 | 97.2 (490/504) [95.6, 98.8] | 96.8 (451/466) [95.1, 98.5] | 97.0 (490/505) [95.2, 98.2] | 97.0 (451/465) [95.0, 98.2] | 97.0 (941/970) [95.7, 97.9] |
| R2 | 491 | 454 | 14 | 13 | 97.4 (491/504) [95.8, 99.0] | 97.0 (454/468) [95.4, 98.7] | 97.2 (491/505) [95.4, 98.3] | 97.2 (454/467) [95.3, 98.4] | 97.2 (945/972) [96.0, 98.1] |
| Aneurysms 3–5 mm | | | | | | | | | |
| R1 | 409 | 451 | 7 | 7 | 98.3 (409/416) 96.8, 99.9] | 98.5 (451/458) [97.3, 99.6] | 98.3 (409/416) [96.6, 99.2] | 98.5 (451/458) [96.9, 99.3] | 98.4 (860/874) [97.3, 99.0] |
| R2 | 411 | 454 | 8 | 5 | 98.8 (411/416) [97.4, 100] | 98.3 (454/462) [97.1, 99.5] | 98.1 (411/419) [96.3, 99.0] | 98.9 (454/459) [97.5, 99.5] | 98.5 (865/878) [97.5, 99.1] |
| Aneurysms <3 mm | | | | | | | | | |
| R1 | 81 | 451 | 8 | 7 | 92.0 (81/88) [85.1, 99.0] | 98.3 (451/459) [96.9, 99.6] | 91.0 (81/89) [83.3, 95.4] | 98.5 (451/458) 96.9, 99.3] | 97.3 (532/547) 95.5, 98.3] |
| R2 | 80 | 454 | 6 | 8 | 90.9 (80/88) [83.7, 98.1] | 98.7 (454/460) [97.7, 99.7] | 93.0 (80/86) [85.6, 96.8] | 98.3 (454/462) [96.6, 99.1] | 97.4 (534/548) [95.8, 98.5] |
| Unruptured small aneurysms | | | | | | | | | |
| Overall | | | | | | | | | |
| R1 | 187 | 451 | 1 | 20 | 90.3 (187/207) 85.7, 95.0] | 99.8 (451/452) [99.3, 100] | 99.5 (187/188) [97.1, 99.9] | 95.8 (451/471) [93.5, 97.2] | 96.8 (638/659) [95.2, 97.9] |
| R2 | 187 | 454 | 0 | 20 | 90.3 (187/207) [85.5, 95.2] | 100 (454/454) [99.2, 100] | 100 (187/187) [98.0, 100] | 95.8 (454/474) [93.6, 97.3] | 97.0 (641/661) [95.4, 98.0] |
| Aneurysms 3–5 mm | | | | | | | | | |
| R1 | 97 | 451 | 0 | 5 | 95.1 (97/102) [89.6, 100] | 100 (451/451) [99.2, 100] | 100 (97/97) 96.2, 100] | 98.9 (451/456) [97.5, 99.5] | 99.1 (548/553) [97.9, 99.6] |
| R2 | 99 | 454 | 0 | 3 | 97.1 (99/102) [92.1, 100] | 100 (454/454) [99.2, 100] | 100 (99/99) [96.3, 100] | 99.3 (454/457) [98.1, 99.8] | 99.5 (553/556) [98.4, 99.8] |
| Aneurysms <3 mm | | | | | | | | | |
| R1 | 90 | 451 | 1 | 15 | 85.7 (90/105) 77.9, 93.5] | 99.8 (451/452) [99.3, 100] | 98.9 (90/91) [94.0, 99.8] | 96.8 (451/466) [94.8, 98.0] | 97.1 (541/557) [95.4, 98.2] |
| R2 | 88 | 454 | 0 | 17 | 83.8 (88/105) [75.4, 92.2] | 100 (454/454) [99.2, 100] | 100 (88/88) [95.8, 100] | 96.4 (454/471) [94.3, 97.7] | 97.0 (542/559) [95.2, 98.1] |

Note.—Data in parentheses are numerator and denominator; data in brackets are 95% confidence intervals. FN = false-negative finding, FP = false-positive finding, NPV = negative predictive value, PPV = positive predictive value, R1 = reader 1, R2 = reader 2, TN = true-negative finding, TP = true-positive finding.

in the left ophthalmic artery segment of the internal carotid artery in a 64-year-old male patient was missed because of overshooting bone subtraction (Fig 3c, 3d). We also found 58.8% (20 of 34) and 60.6% (20 of 33) missed aneurysms were unruptured, evaluated by two readers. Common locations of false-positive aneurysms found by reader 1 and reader 2 were internal carotid artery (six and four false-positive aneurysms, respectively), posterior communicating artery (four and two false-positive aneurysms, respectively), and anterior choroidal artery (two and three false-positive aneurysms). Common locations of missed aneurysms found by reader 1 and reader 2 were middle cerebral artery (eight and five missed aneurysms, respectively), anterior communicating artery (seven and six missed aneurysms, respectively), ophthalmic artery segment of internal carotid artery (five and six missed aneurysms, respectively), cavernous segment of internal carotid artery (four and five missed aneurysms, respectively), and posterior cerebral artery (three and three missed aneurysms, respectively).

## Discussion

In our study, relatively high sensitivity, specificity, and accuracy for cerebral CT angiography were found for detection of small aneurysms, even with aneurysms smaller than 3 mm. These findings further supported the role of CT angiography in detection of small cerebral aneurysms in routine clinical practice. Although many previous studies support our results (25–28), some lower sensitivities of CT angiography for detection of small aneurysms were reported, especially for aneurysms less than 3 mm (29–34). Among these studies, the sample size, CT scanners (eg, 16-, 64-, or 320-section multi–detector row or dual-energy CT), image acquisition protocol (eg, volume, concentration, and injection rate of contrast agent), and image quality varied and could account for the discrepancy between studies. In our study, CT images were acquired by using advanced CT

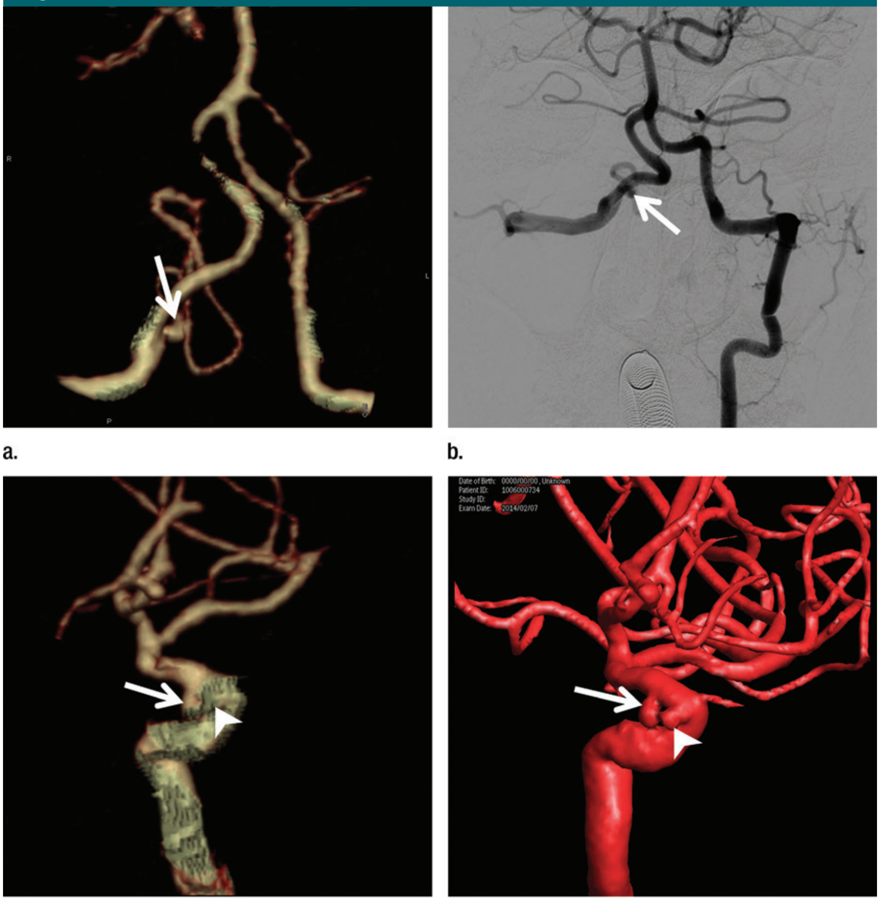
**Table 4**

**Diagnostic Performance of CT Angiography in Detecting Small Aneurysms at Different Locations**

| Parameter | Results (No. of Aneurysms) | | | | Test Performance (%) | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | TP | TN | FP | FN | Sensitivity | Specificity | PPV | NPV | Accuracy |
| Anterior circulation | | | | | | | | | |
| Overall | | | | | | | | | |
| R1 | 611 | 451 | 14 | 28 | 95.6 (611/639) [93.8, 97.4] | 97.0 (451/465) [95.3, 98.6] | 97.8 (611/625) [96.3, 98.7] | 94.2 (451/479) [91.7, 95.9] | 96.2 (1062/1104) [94.9, 97.2] |
| R2 | 612 | 454 | 12 | 27 | 95.8 (612/639) [93.9, 97.6] | 97.4 (454/466) [95.9, 99.0] | 98.1 (612/624) [96.7, 98.9] | 94.4 (454/481) [92.0, 96.1] | 96.5 (1066/1105) [95.2, 97.4] |
| ICA | | | | | | | | | |
| R1 | 140 | 451 | 8 | 12 | 92.1 (140/152) [86.6, 97.6] | 98.3 (451/459) [97.1, 99.5] | 94.6 (140/148) [89.7, 97.2] | 97.4 (451/463) [95.5, 98.5] | 96.7 (591/611) 95.0, 97.9] |
| R2 | 138 | 454 | 7 | 14 | 90.8 (138/152) [85.1, 96.5] | 98.5 (454/461) [97.4, 99.6] | 95.2 (138/145) [90.4, 97.6] | 97.0 (454/468) [95.0, 98.2] | 96.6 (592/613) [94.8, 97.8] |
| ACA | | | | | | | | | |
| R1 | 36 | 451 | 0 | 0 | 100 (36/36) [90.4, 100] | 100 (451/451) [99.2, 100] | 100 (36/36) [90.4, 100] | 100 (451/451) [99.2, 100] | 100 (487/487) [99.2, 100] |
| R2 | 36 | 454 | 1 | 0 | 100 (36/36) [90.4, 100] | 99.8 (454/455) [98.8, 100] | 97.3 (36/37) [86.2, 99.5] | 100 (454/454) [99.2, 100] | 99.8 (490/491) [98.9, 100] |
| MCA | | | | | | | | | |
| R1 | 81 | 451 | 2 | 8 | 91.0 (81/89) [82.7, 99.4] | 99.6 (451/453) [98.7, 100] | 97.6 (81/83) [91.6, 99.3] | 98.3 (451/459) [96.6, 99.1] | 98.2 (532/542) [96.6, 99.0] |
| R2 | 84 | 454 | 0 | 5 | 94.4 (84/89) [86.6, 100] | 100 (454/454) [99.2, 100] | 100 (84/84) [95.6, 100] | 98.9 (454/459) [97.5, 99.5] | 99.1 (538/543) [97.9, 99.6] |
| AcoA | | | | | | | | | |
| R1 | 186 | 451 | 0 | 7 | 96.4 (186/193) [93.1, 99.7] | 100 (451/451) [99.2, 100] | 100 (186/186) [98.0, 100] | 98.5 (451/458) [96.9, 99.3] | 98.9 (637/644) [97.8, 99.5] |
| R2 | 187 | 454 | 2 | 6 | 96.9 (187/193) [93.7, 100] | 99.6 (454/456) [99.0, 100] | 98.9 (187/189) [96.2, 99.7] | 98.7 (454/460) [97.2, 99.4] | 98.8 (641/649) [97.6, 99.4] |
| PcoA | | | | | | | | | |
| R1 | 168 | 451 | 4 | 1 | 99.4 (168/169) [96.8, 100] | 99.1 (451/455) [98.3, 100] | 97.7 (168/172) [94.2, 99.1] | 99.8 (451/452) [98.8, 100] | 99.2 (619/624) [98.1, 99.7] |
| R2 | 167 | 454 | 2 | 2 | 98.8 (167/169) [95.6, 100] | 99.6 (454/456) [99.0, 100] | 98.8 (167/169) [95.8, 99.7] | 99.6 (454/456) [98.4, 99.9] | 99.4 (621/625) [98.4, 99.8] |
| Posterior circulation | | | | | | | | | |
| Overall | | | | | | | | | |
| R1 | 66 | 451 | 2 | 6 | 91.7 (66/72) [83.5, 99.9] | 99.6 (451/453) [98.9, 100] | 97.1 (66/68) [89.9, 99.2] | 98.7 (451/457) [97.2, 99.4) | 98.5 (517/525) [97.0, 99.2] |
| R2 | 66 | 454 | 2 | 6 | 91.7 (66/72) [83.5, 99.9] | 99.6 (454/456) [99.0, 100] | 97.1 (66/68) [89.9, 99.2] | 98.7 (454/460) [97.2, 99.4] | 98.5 (520/528) [97.0, 99.2] |
| VBA | | | | | | | | | |
| R1 | 26 | 451 | 1 | 1 | 96.3 (26/27) [80.3, 100] | 99.8 (451/452) [99.3, 100] | 96.3 (26/27) [81.7, 99.3] | 99.8 (451/452) [98.8, 100] | 99.6 (477/479) [98.5, 99.9] |
| R2 | 25 | 454 | 1 | 2 | 92.6 (25/27) [75.6, 100] | 99.8 (454/455) [99.3, 100] | 96.2 (25/26) [81.1, 99.3] | 99.6 (454/456) [98.4, 99.9] | 99.4 (479/482) [98.2, 99.8] |
| PCA | | | | | | | | | |
| R1 | 11 | 451 | 0 | 3 | 78.6 (11/14) [46.4, 100] | 100 (451/451) [99.2, 100] | 100 (11/11) [74.1, 100] | 99.3 (451/454) [98.1, 99.8] | 99.4 (462/465) [98.1, 99.8] |
| R2 | 11 | 454 | 1 | 3 | 78.6 (11/14) [46.4, 100] | 99.8 (454/455) [99.3, 100] | 91.7 (11/12) [64.6, 98.5] | 99.3 (454/457) [8.1, 99.8] | 99.1 (465/469) [97.8, 99.7] |
| CA | | | | | | | | | |
| R1 | 29 | 451 | 1 | 2 | 93.5 (29/31) [78.6, 100] | 99.8 (451/452) [99.3, 100] | 96.7 (29/30) [83.3, 99.4] | 99.6 (451/453) [98.4, 99.9] | 99.4 (480/483) [98.2, 99.8] |
| R2 | 30 | 454 | 0 | 1 | 96.8 (30/31) [82.8, 100] | 100 (454/454) [99.2, 100] | 100 (30/30) [88.7, 100] | 99.8 (454/455) [98.8, 100] | 99.8 (484/485) [98.8, 100] |

Note.—Data in parentheses are numerator and denominator; data in brackets are 95% confidence intervals. ACA = anterior cerebral artery, AcoA = anterior communicating artery, CA = cerebellar artery, FN = false-negative finding, FP = false-positive finding, ICA = internal carotid artery, MCA = middle cerebral artery, NPV = negative predictive value, PCA = posterior cerebral artery, PcoA = posterior communicating artery, PPV = positive predictive value, R1 = reader 1, R2 = reader 2, TN = true-negative finding, TP = true-positive finding, VBA = vertebral and basilar artery.

**Figure 3**



a. b. c. d.

**Figure 3:** Two misdiagnosed aneurysms in two patients. **(a)** Volume-rendered CT angiography image shows reported aneurysm at right posterior inferior cerebellar artery (arrow) with maximal diameter of 3.8 mm measured at CT angiography in a 43-year-old man, and **(b)** conventional DSA image does not show the aneurysm (arrow) in that patient. **(c)** Volume-rendered CT angiography image shows one aneurysm at the left ophthalmic artery segment of internal carotid artery (arrow) in a 64-year-old man, whereas **(d)** volume-rendered 3D DSA image clearly shows two adjacent aneurysms in this location: one is 3.4 mm (arrow) and the other is 2.5 mm (arrowhead) in diameter, respectively. CT angiography missed the smaller aneurysm (arrowhead in **c**) because of overshooting bone removal.

scanners with 0.6-mm spatial resolution and were freely adjusted, rotated, and reformatted on a 3D workstation to provide optimal views of the aneurysms. Target vessel reformation was performed for lesions that were highly suspected of being aneurysms. Good CT angiography image quality helped to reduce missed aneurysms, especially with aneurysms smaller than 3 mm. In this cohort, 86.9% (1187 of 1366) of patients had intracranial hemorrhage on CT images. In our experience, the readers' prior probability of finding an aneurysm for the reader is much higher with known nontraumatic subarachnoid hemorrhage, which may be a weakness of this study. Additionally, in this retrospective study, some CT angiography images negative for aneurysms were not followed by DSA, which may inflate the sensitivity, negative predictive value, and accuracy of CT angiography to some extent. Taken together, these factors resulted in relatively high diagnostic accuracy in this study.

Although a relatively good diagnostic accuracy of CT angiography for detection of small cerebral aneurysms was obtained, 11.4%–13% aneurysms smaller than 3 mm were missed in this study. These false-positive and false-negative findings deserve further reflection. In this study, a false-positive aneurysm was observed at CT angiography because the target vessel angiography and rotational 3D DSA were not performed in that patient. Previous studies (35,36) concluded that 3D DSA was superior to two-dimensional DSA to detect and delineate cerebral aneurysms. Thus, it is possible that this case could represent a true-positive finding not evident on two-dimensional DSA images but detectable at 3D DSA. Infundibula were diagnosed as small aneurysms because the vessels originating from the apex of infundibula were not clearly viewed at CT angiography in those cases. Although CT angiography could help to correctly depict some infundibula, it was difficult to distinguish infundibula from small aneurysms in many cases.

Our analysis showed that 64.7% (22 of 34) and 75.8% (25 of 33) of missed aneurysms were less than 3 mm in diameter and that 55.9% (19 of 34) and 57.6% (19 of 33) of false-negative aneurysms were found in patients who had two or more aneurysms. With the bone-subtraction technology used in this study, an excellent sensitivity of more than 90% was obtained for the detection of internal carotid artery aneurysms. However, several aneurysms were still missed in the ophthalmic artery segment and cavernous segment of the internal carotid artery. Another reason for missing small aneurysms is their presence in uncommon locations that are easily overlooked, for instance the posterior inferior cerebellar artery, the distal middle cerebral artery, and the anterior choroidal artery. The small aneurysms located at the distal segment of intracranial arteries are also prone to be overlooked, resulting in a lower sensitivity. This could account for the unsatisfactory sensitivity for detection of aneurysms in the posterior cerebral artery by using CT angiography in this study. Poor image quality caused by motion artifacts or inappropriate

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delay time of CT angiography can also lead to missed aneurysms, even aneurysms larger than 5 mm. Aneurysms in patients with other cerebrovascular diseases such as moyamoya disease, arteriovenous malformation, and cerebrovascular occlusion might have a higher probability of false-negative diagnosis. In addition, for both readers most missed small aneurysms (58.8% [20 of 34] and 60.6% [20 of 33]), especially those smaller than 3 mm, were unruptured in our study, and there was an inferior sensitivity of CT angiography in detecting unruptured small aneurysms compared with ruptured small aneurysms. Unlike ruptured aneurysms, small unruptured aneurysms may get less attention and have lower reader confidence when evaluated at CT angiography by radiologists. In addition, dissecting aneurysms without an aneurysmal sac might be sometimes missed at CT angiography even though the long diameters were larger than 5 mm. Taken together, aneurysm size, location and number, CT angiography image quality, co-occurring cerebrovascular diseases, and unruptured status may be factors that influence the accuracy of CT angiography in the detection of small cerebral aneurysms.

There are several limitations of our study that need to be considered. First, this was a retrospective study conducted at a single center. It is inevitable that some patients with negative findings at CT angiography did not undergo DSA, which may affect the sensitivity and negative predictive value of CT angiography relative to DSA. Second, spatial resolution of cerebral CT angiography in this study (0.6 mm) was inferior to that of DSA, which may account for the misdiagnosis of infundibula as aneurysms and false-negative diagnosis of some small aneurysms. Last, CT angiography images in our study were acquired by using two different CT scanners and by using slightly different scanning protocols. The effect of different scanners on the diagnostic accuracy of CT angiography for detection of aneurysms requires further investigation.

To conclude, this large cohort study showed that cerebral CT angiography had relatively high diagnostic accuracy for detection of small cerebral aneurysms, although it was less so for aneurysms with a diameter smaller than 3 mm.

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